

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of the Claims

1. (Currently Amended) An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:
 - a) the *dbv* gene cluster encoding the polypeptides required for the synthesis of A40926 (SEQ ID NO: 1);
 - b) a nucleotide sequence encoding the same polypeptides encoded by the *dbv* gene cluster (SEQ ID NO: 1), other than the nucleotide sequence of the *dbv* gene cluster;
 - c) any nucleotide sequence of *dbv* ORFs 1 to 37, encoding the polypeptides of SEQ ID NOS: 2 to 38; and
 - d) a nucleotide sequence encoding the same polypeptides encoded by any of *dbv* ORFs 1 to 37 (SEQ ID NOS: 2 to 38), other than the nucleotide sequence of said ORF.

2. (Currently Amended) ~~An~~ The isolated nucleic acid of claim 1, wherein the comprising a nucleotide sequence is selected from the group consisting of:

- e) a nucleotide sequence of any of *dbv* ORFs 3 to 4, 6 to 10, 18 to 20, 22 to 23, 29 to 30, and 36 (SEQ ID NOS: 4 to 5, 7 to 11, 19 to 21, 23 to 24, 30 to 31, and 37);
- f) a nucleotide sequence encoding the same polypeptide encoded by any of *dbv* ORFs 3 to 4, 6 to 10, 18 to 20, 22 to 23, 29 to 30, and 36 (SEQ ID NOS: 4 to 5, 7 to 11, 19 to 21, 23 to 24, 30 to 31, and 37), other than the nucleotide sequence of said ORF, of said ORF;
- g) a nucleotide sequence encoding a polypeptide that is at least 80%, preferably 86%, more preferably 90%, most preferably 95% or more, identical in amino acid sequence to a polypeptide encoded by any of *dbv* ORFs 3, 6 to 9, 18 to 20, 22 to 23, 29 to 30, and 36 (SEQ ID NOS: 4, 7 to 10, 19 to 21, 23 to 24, 30 to 31, and 37); and
- h) a nucleotide sequence encoding a polypeptide that is at least 87%, preferably 90%, more preferably 95% or more, identical in amino acid sequence to a polypeptide encoded by any of *dbv* ORFs 4 and 10 (SEQ ID NOS: 5 and 11).

3. (Currently Amended) ~~An~~ The isolated nucleic acid according to claim 2 comprising claim 2, wherein the nucleic acid sequence comprises a combination of nucleotide sequences which that encode polypeptides required for the synthesis of the 4-hydroxy-phenylglycine residues of A40926 selected from the group consisting of *dbv* ORFs 1, 2, 5 and 37 ORFs 1, 2, 5, 37 (SEQ ID NOS: 2, 3, 6 and 38), or nucleotide sequences and other nucleotide sequences encoding the same polypeptides, other than the nucleotide sequences of said ORFs.

4. (Currently Amended) ~~An~~ The isolated nucleic acid according to claim 2 comprising claim 2, wherein the nucleic acid sequence comprises a combination of nucleotide sequences which that encode polypeptides required for the synthesis of the 3,5-dihydroxy-phenylglycine residues of A40926 selected from the group consisting of *dbv* ORFs 30 to 34, [[and]] 37 (SEQ ID NOS: 31 to 35, and 38), or nucleotide sequences and other nucleotide sequences encoding the same polypeptides, other than the nucleotide sequences of said ORFs.

5. (Currently Amended) An The isolated nucleic acid according to claim 2 comprising claim 2, wherein the nucleic acid sequence comprises a combination of nucleotide sequences which that encode polypeptides required for the synthesis of the heptapeptide skeleton of A40926 selected from the group consisting of dbv ORFs 16, 17, 25, 26, 36 and 36 (SEQ ID NOS: 17 to 18, 26 to 27, and 37), or nucleotide sequences and other nucleotide sequences encoding the same polypeptides; other than the nucleotide sequences of said ORFs.

6. (Currently Amended) An The isolated nucleic acid according to claim 2 comprising claim 2, wherein the nucleic acid sequence comprises a nucleotide sequence which that encodes a polypeptide required for the chlorination of the aromatic residues of amino acids 3 and 6 of A40926 selected from the group consisting of dbv ORF 10 (SEQ ID NO: 11), or nucleotide sequences and other nucleotide sequences encoding the same polypeptide, other than the nucleotide sequence of said ORF.

7. (Currently Amended) An The isolated nucleic acid according to claim 2 comprising claim 2, wherein the nucleic acid sequence comprises a nucleotide sequence which that encodes a polypeptide required for the β -hydroxylation of the tyrosine residue of amino acid 6 of A40926 selected from the group consisting of dbv ORF 28 ORF 28 (SEQ ID NO: 29), or nucleotide sequences and other nucleotide sequences encoding the same polypeptide, other than the nucleotide sequence of said ORF.

8. (Currently Amended) An The isolated nucleic acid according to claim 2 comprising claim 2, wherein the nucleic acid sequence comprises a combination of nucleotide sequences which that encode polypeptides required for the cross-linking of the aromatic residues of amino acids at positions 2 and 4, 4 and 6, 1 and 3, and 5 and 7 of A40926 selected from the group consisting of dbv ORFs 11 ORFs 11 to 14 (SEQ ID NOS: 12 to 15), or nucleotide sequences and other nucleotide sequences encoding the same polypeptides, other than the nucleotide sequences of said ORFs.

9. (Currently Amended) An The isolated nucleic acid according to claim 2 comprising claim 2, wherein the nucleic acid sequence comprises a combination of nucleotide sequences which that encode polypeptides required for the addition and formation of the N-acyl glucuronamine residue of A40926 selected from the group consisting of ORFs 9, 23 and 23, 29 (SEQ ID NOS: 10, 24 and 30), or nucleotide sequences and other nucleotide sequences encoding the same polypeptides, other than the nucleotide sequences of said ORFs.

10. (Currently Amended) An The isolated nucleic acid according to claim 2 comprising claim 2, wherein the nucleic acid sequence comprises a nucleotide sequence which that encodes a polypeptide required for the attachment of the mannosyl residue of A40926 selected from the group consisting of *dbv* ORF 20 (SEQ ID NO: 21), or nucleotide sequences and other nucleotide sequences encoding the same polypeptide, other than the nucleotide sequence of said ORF.

11. (Currently Amended) An The isolated nucleic acid according to claim 2 comprising claim 1, wherein the nucleic acid sequence comprises a nucleotide sequence which that encodes a polypeptide required for the N-methylation of A40926 selected from the group consisting of *dbv* ORF 27 (SEQ ID NO: 28), or nucleotide sequences and other nucleotide sequences encoding the same polypeptide, other than the nucleotide sequence of said ORF.

12. (Currently Amended) An The isolated nucleic acid according to claim 2 comprising claim 2, wherein the nucleic acid sequence comprises a combination of nucleotide sequences which that encode polypeptides required for export of A40926 or some of its precursors outside of the cytoplasm and for conferring resistance to A40926 to the producing strain selected from the group consisting of *dbv* ORFs 7, 18, 19, 24 and 24, 35 (SEQ ID NOS: 8, 19 to 20, 25 and 36), or nucleotide sequences and other nucleotide sequences encoding the same polypeptides, other than the nucleotide sequences of said ORFs.

13. (Currently Amended) ~~An~~ The isolated nucleic acid according to ~~claim 2 comprising claim 2, wherein the nucleic acid sequence comprises a combination of nucleotide sequences which that encode polypeptides required for regulating the expression of one or more genes of the dbv gene cluster selected from the group consisting of dbv ORFs 3, 4, 6 and 6, 22 (SEQ ID NOS: 4, 5, 7 and 23), or nucleotide sequences and other nucleotide sequences encoding the same polypeptides, other than the nucleotide sequences of said ORFs.~~

14. (Currently Amended) ~~An~~ The isolated nucleic acid according to ~~claim 1 comprising claim 1, wherein the nucleic acid sequence comprises a nucleotide sequence consisting of comprises the dbv gene cluster encoding the polypeptide required for the synthesis of a A40926 A40926,~~ wherein an in frame deletion has been introduced in the nucleotide sequence encoding the polypeptides required for the attachment of the mannosyl residue.

15. (Currently Amended) ~~An~~ The isolated nucleic acid according to claim 1 comprising a nucleotide sequence carrying at least one extra-copy of at least one of the dbv ORFs 1 to 37 (SEQ ID NOS: 2 to 38) or of a nucleotide sequence encoding the same polypeptides encoded by said dbv ORF, other than the nucleotide sequence of said dbv ORF.

16. (Canceled)

17. (Currently Amended) A recombinant DNA vector which comprises a DNA sequence as ~~defined in any of claims 1 to 15~~ selected from the group consisting of claim 1.

18. (Currently Amended) ~~A~~ The recombinant vector according to ~~claim 17 which claim 17,~~ wherein the recombinant vector is an ESAC vector.

19. (Canceled)

20. (Canceled)

21. (Currently Amended) A method for increasing production of A40926 by a microorganism capable of producing A40926 or a precursor thereof by means of a biosynthetic pathway, said method comprising:

- a) transforming with a recombinant DNA vector ~~of claim 17~~ a microorganism that produces A40926 or a A40926 precursor by means of a biosynthetic pathway, wherein said DNA vector codes for the expression of an activity that is rate limiting in said pathway;
- b) culturing said microorganism transformed with said vector under conditions suitable for cell growth, expression of ~~said gene~~ said gene, and production of said antibiotic or antibiotic precursor.

22. (Canceled)

23. (Canceled)

24. (Original) A transformed A40926-producing microorganism having A40926 biosynthetic genes in its genome wherein at least one of the A40926 biosynthetic genes, selected from *dbv* ORFs 1 to 37 (SEQ ID NOS: 2 to 38), is disrupted.

25. (Currently Amended) ~~A transformed~~ The transformed microorganism according to claim 24, wherein the biosynthetic gene which is disrupted is the gene involved in the attachment of the mannosyl residue.

26. (Canceled)

27. (Currently Amended) A method for producing a glycopeptide different from A40926 or a precursor thereof, comprising the steps of which consists in:

a) (i) transforming with a recombinant DNA vector a microorganism that produces a glycopeptide or a glycopeptide precursor different from A40926 or a precursor thereof by means of a biosynthetic pathway, said vector or portion thereof comprising one or more nucleotide sequences sequence(s) of any of claim 1 to 13, coding for the expression of one or more polypeptides that modify polypeptide(s) that modifies(y) said glycopeptide or glycopeptide precursor; and

(ii) culturing said microorganism transformed with said vector under conditions suitable for cell growth, expression of said gene and production of said antibiotic or antibiotic precursor;

or

b) (i) transforming with a recombinant DNA vector a microorganism, said vector comprising one or more nucleotide sequences sequence(s) of any of claims 1 to 13, coding for one or more polypeptide(s) active polypeptides that modifies(y) modifies a glycopeptide or glycopeptide precursor, wherein (active polypeptide(s)), and said microorganism being is selected from among those that do not produce glycopeptides or glycopeptide precursors and that can efficiently express the introduced one or more nucleotide sequences; sequence(s);

(ii) preparing a cell extract or cell fraction of said microorganism under conditions suitable for the presence of the one or more active polypeptides active polypeptide(s), said cell extract or cell fraction containing at least said one or more active polypeptides active polypeptide(s); and

(iii) adding a glycopeptide or glycopeptide precursor to said cell extract or cell fraction[[,]] to form a mixture; and

(iv) incubating said mixture under conditions where said one or more active polypeptides active polypeptide(s) can modify said glycopeptide or glycopeptide precursor.

28. (Currently Amended) An isolated polypeptide comprising a polypeptide sequence involved in the biosynthetic pathway of A40926 selected from the group consisting of

- a) an ORF polypeptide encoded by any of *dbv* ORFs 1 to 37 (SEQ ID NOS: 2 through 38) or a polypeptide which is[[,]] identical in amino acid sequence to an ORF polypeptide encoded by any of *dbv* ORFs 1 to 37 (SEQ ID NOS: 2 through 38), ~~preferably by any one of the *dbv* ORFs 3 to 4, 6 to 10, 18 to 20, 22 to 23, 29 to 30 (SEQ ID NOS: 4 to 5, 7 to 11, 19 to 21, 23 to 24, 30 to 31 and 37);~~
- b) a polypeptide which is at least 80%, ~~preferably 86%, more preferably 90%, most preferably 95% or more,~~ identical in amino acid sequence to a polypeptide encoded by any of *dbv* ORFs 3, 6 to 9, 18 to 20, 22 to 23 , 29 to 30 and 36 (SEQ ID NOS.: 4, 7 to 10, 19 to 21, 23 to 24, 30 to 31 and 37); and
- c) a polypeptide which is at least 87%, ~~preferably 90%, more preferably 95% or more,~~ identical in amino acid sequence to a polypeptide encoded by any of *dbv* ORFs 4 and 10 (SEQ ID NOS: 5 and 11).

29. (Canceled)